connective-tissue hypertrophy seen in the last type. This type clinically is seen usually as a tumor which may or may not cause any other inconvenience than that of pressure. It usually is an encapsulated tumor in the thyroid, and can be shelled out. However, when the encysted or encapsulated fœtal adenomas occur, the tissue may degenerate from some unknown reason, or perhaps from circulatory changes due to the thickened capsule, and then the products may be rapidly taken up by the lymphatics and thrown into the circulation, giving symptoms of hyperthyroidism. This type may be termed fœtal adenoma of the thyroid (thyroidea fœtalis adenoma tosa) (Figs. 6 and 7*a*).

RESUME. 1. The process of goitre may be a process of reversion of the thyroid gland to some former function.

2. Hyperthyroidism is a toxemia the result of absorption of the products of the hyperactive thyroid.

3. The stimulus causing the hyperactivity may be the same that stimulated the thyroid to activity in primitive man.

4. This stimulus was then probably a normal stimulus to the gland, just as we have normal stimuli for glandular activity in man in his present condition.

5. This stimulus may still be present in the food or water, formed through some process in the intestine or in the metabolism of the body, or it may exist in the air.

6. The types of goitre are probably not types but stages in a general process.

7. Goitre may be classified upon a pathological basis as follows: (*a*) Cystic goitre (thyroidea cystica) (Fig. 3). (*b*) Hypertrophic parenchymatous goitre (thyroidea parenchymatosa hypertrophica) (Fig. 4). (*c*) Papillary cystic goitre (thyroidea cystica papillare) (Fig. 5 *a* and *b*). (*d*) Hypertrophic fœtal thyroid (thyroidea fœtalis hypertrophica). (*e*) Fœtal adenoma of the thyroid (thyroidea fœtalis adenomatosa) (Fig. 6).

8. Hyperthyroidism always occurs in *b* and *c*, and may occur in *e* (Figs. 4, 5, and 6).

THE NATURE, DIAGNOSIS, AND TREATMENT OF METABOLIC OSTEO-ARTHRITIS.

SO-CALLED RHEUMATOID ARTHRITIS, ARTHRITIS DEFORMANS, ETC.

BY P. WILLIAM NATHAN, M.D.
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IN a series of papers on the classification of the joint diseases generally known as rheumatoid arthritis, arthritis deformans, etc., published in this journal,[1] this supposed group of joint diseases was shown to be composed of a number of dissimilar diseases. It was further shown that the joint diseases generally, and with them the so-called rheumatoid affections, like the diseases of other organs, could be divided into two fundamental classes—the inflammations (infections), and the degenerations (trophic diseases). Moreover, it was shown that the joint diseases could be further subdivided, according to the original location of the disease, into synovial forms (arthritis) and osseous forms (osteo-arthritis), so that by the use of four simple and definite names we could indicate a definite clinical entity corresponding to definite pathological changes, without having recourse to a long description of the malady in order to make our meaning clear to others.

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[1] January, April, December, 1906.

Thus, there is: (1) Infectious arthritis, an infectious joint disease involving the soft parts primarily; (2) infectious osteo-arthritis, an infection involving the bones primarily; (3) trophic arthritis, a degenerative joint disease involving the synovia only; and (4) trophic osteo-arthritis, one involving both the bones and soft parts. These names, it was shown, could be made still more definite when the etiology is known; so, for instance, pneumococcic osteo-arthritis, a pneumococcic infection involving the osseous structure of the joints, having the general characters of infectious osteo-arthritis; or neurotic osteo-arthritis, a trophic degenerative change involving the osseous joint structures due to nerve lesion—as in tabes, syringomyelitis, etc. In the last paper of the series it was shown that by means of this classification the so-called rheumatoid conditions could be differentiated from one another clinically.

However, as these papers were simply preliminary, giving only a general view of the subject, many details of the pathology, etiology, and the symptoms of the various diseases were purposely omitted in order to simplify the subject. This was particularly the case with the disease designated as metabolic osteo-arthritis and corresponding to Schuchardt's arthritis nodosa, Baumler's arthritis deformans, and Goldthwait's atrophic arthritis, of which only a few leading features were discussed. As this disease presents many interesting features which are still misunderstood, or the subject of controversy, and, as I believe, the results of my investigations are definite enough to give us a more intelligent conception of the disease, I purpose to deal with this subject, in detail, in the present communication.

In studying a disease of an organ the first point to be decided is, Is it a local condition, causing secondary general symptoms, or is the disease a part of some general condition, that is, is the disease primary or secondary? If the disease of the organ is primary, the study of the pathology and symptomatology as they refer to the organ may lead to a better understanding of the etiology and pathogenesis of the disease. When, however, the disease of the organ is secondary or a part of some general morbid process, the study of the local condition can, of course, never lead to a true conception of the disease itself.

Though the majority of observers have looked upon metabolic osteo-arthritis as a joint disease caused by some uniform general abnormality, the search for the cause and pathogenesis has nearly always been confined to the joints only. It is true that for many years a general metabolic abnormality (excess of uric acid) has been considered the cause of the joint disease and of the general condition; but since it has been shown[2] that uric acid has nothing to do with the disease, only the local condition has been considered. If, as has been assumed, metabolic osteo-arthritis is a general disease, it is futile to expect to discover the pathogenesis or cause by studying the joint condition only. The most we could hope for would be a better understanding of the local condition. But not even the joint condition has been carefully studied. The descriptions of the symptoms and course of the disease to be found in the general literature are either inadequate or inaccurate; and the pathology, studied in subjects (dead of some intercurrent malady) without a history of the joint disease, or by means of museum specimens without any clinical data whatsoever, is seriously misconceived. In the present instance it is, therefore, necessary to arrive at a definite understanding of the local condition before we can discuss its relation to the general manifestations of the disease or of the disease itself. Hence, the study of the subject is divided into the following parts:

1. The study of the joint conditions: (*a*) to establish a clinical entity; (*b*) the diagnosis of the joint condition, that is, its differentiation from all other joint diseases.

2. The pathology of the joint disease. Not the pathology of a general disease is intended, but only the anatomical findings in the joints of individuals who have presented, during life, the joint condition herein described.

3. Having established a definite joint condition with definite and easily recognizable anatomical changes, the general symptoms presented by individuals with such a joint abnormality will be discussed.

4. From the study of the joint symptoms and the general symptoms, I shall attempt to decide whether the disease is primarily a joint disease causing general symptoms or a general disease with joint involvement.

5. Granting the disease is general, the question then to be decided is, the nature of the general condition. Is it a definite and specific abnormality, or might not, as is so often the case with other joint diseases, a number of dissimilar general conditions be instrumental in its production.

6. These points having been more or less satisfactorily settled, a method of treatment which in my hands has been of benefit, will be detailed.

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[2] McCrudden, Uric Acid, Boston, 1905.

THE JOINT SYMPTOMS. *Muscular Atrophy.* Muscular atrophy is always a very early symptom of joint disease, and not infrequently can be detected before the other physical signs of joint disease present themselves. In no other joint affection, however, does it appear so early, or is it so marked as in metabolic osteo-arthritis. Not only does it appear early, but it progresses more rapidly and quite out of proportion to the other joint manifestations. At times it becomes extreme; and when the disease attacks the joints of the hands and fingers, which is usually the case, the condition might be mistaken for one of paralysis. Indeed, when flexion deformity predominates, the hands may exactly resemble the paralytic claw hand (Fig. 1). Though the muscular atrophy is not always so intense, it is very marked in the majority of cases; and whatever may be its cause in other joint diseases, it seems to me quite improbable that this extreme atrophy, which is present so early and whilst the limb is still in condition to perform at least some of its functions, should be due to the joint disease alone.

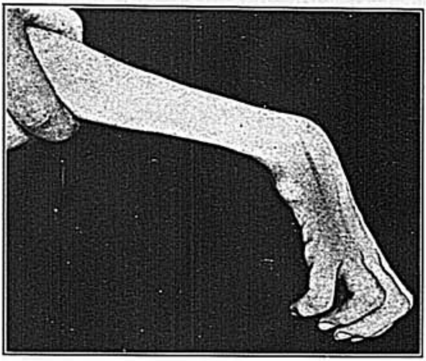

FIG. 1.—Pure flexion deformity in metabolic osteo-arthritis in a girl aged ten years. There is no swelling; the hand resembles the paralytic claw hand. The disease had existed for four years.

Subjective Symptoms. The earliest symptom complained of by the patient is joint stiffness. This is much more pronounced when the disease begins in the hands, and especially so in those engaged in pursuits which require fine manual adjustments. The stiffness is said to be more severe upon arising in the morning, and gradually disappears to a certain extent during the day. As time goes on, however, it extends over longer and longer periods, and finally becomes constant. If the joints are examined during this time, before joint swelling and the signs of actual joint irritation have made their appearance, it will be found that passive motion is hardly, if at all, limited, though the patient complains of the stiffness. It, therefore, seems more probable that what the patient calls stiffness is really weakness. Indeed, the more intelligent patients do not complain of stiffness, but of gradually increasing weakness. With the weakness various other subjective symptoms are present. Patients complain of formication, etc., and pain.

Pain. Pain is a most variable symptom. It not only varies in the different individuals, but in the different joints of the same individual. In some joints the disease runs its course with slight or no pain at all; in some it is severe but transitory; in others it is intense, constant night and day, and unaffected by immobilization for weeks or months. The character of the pain is similarly variable; it may be dull or sharp and lancinating, and may or may not be increased by passive motion. When present it is always increased by pressure upon the bone near the joint.

As all these patients are chronic invalids and many of them present decided signs of functional nervous derangement, I have often been unable to decide whether or not the pain is due to nervous influences. In some cases I indeed suspected an hysterical element; but in the majority of them the long-continued sleepless nights and the total failure of suggestive treatment (hypodermic injections of water, etc.) have convinced me that the pain is real and not imaginary; the more so as I have known it to be very intense in patients with absolutely no neurotic symptoms. In one case (a lady, aged thirty-five years), with all the joints involved except the spine and maxillæ, the pain in the ankles continued intense for a number of weeks, and nothing relieved her but opium given in suppositories. After the pain ceased the patient discontinued the suppositories voluntarily.

So far as I can make out, the pain does not correspond to any particular stage of the disease. It is usually present early, and in the majority of cases is most severe when the disease is most active. It usually subsides with the subsidence of the joint destruction, but it may be mild in the earlier stages and very severe later on. In certain forms of the disease in children there is practically no pain at all.

Joint Swelling. The peculiar form of swelling which occurs in metabolic osteo-arthritis has been considered by the earlier English and French writers the most characteristic symptom of the disease. Because of it, Heygarth named the condition nodosity of joints; Trousseau called it rheumatisme noueux; and still more recently Schuchardt called it arthritis nodosa. There can be no question that the peculiar nodular swelling is a very characteristic symptom; but the swelling is not always nodular; if present at all, it is only present for a limited time; and it may be masked by joint effusion.

Weakness or stiffness, pain, and other subjective symptoms precede the joint swelling by a variable length of time. This interval depends upon two factors: (1) The rapidity of the progress made by the disease; (2) the external mechanical conditions. In some cases atrophy and weakness progress rapidly; the affected extremities are painful and soon become so weak that active function is impossible. In these, when the disease attacks the upper extremity, it runs its course uncomplicated by mechanical joint irritation, and the characteristic joint swelling soon makes its appearance. In others the weakness is very slowly progressive, and in those whose occupation does not entail the constant use of the affected parts, the preliminary joint symptoms may exist for some time before joint swelling. On the other hand, in those who use the extremities constantly or violently the joint swelling soon makes its appearance whether the disease progresses rapidly or not.

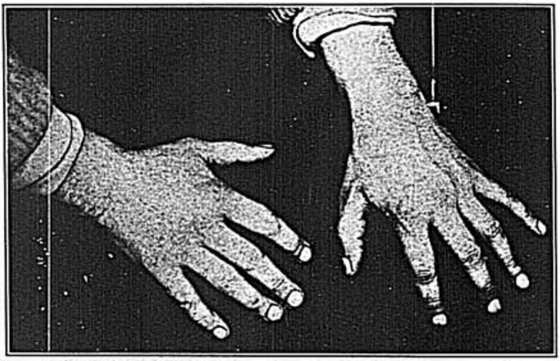

FIG. 2.—The hands in a very early stage of metabolic osteo-arthritis. There is no effusion, but a very slight spindle-form swelling. The fingers are just beginning to deviate laterally.

Not only is the period before the advent of joint swelling variable in correspondence with the internal and external conditions, but the character of the swelling depends upon them. Thus, in those cases with severe, rapid progress and early cessation of function, it comes on gradually, is at first spindle shaped (Fig. 2), and later, due to a thickening of the soft parts, assumes the characteristic nodular form (Figs. 3 and 4). When the disease progresses more gradually and more slowly and the early subjective symptoms are milder, it permits of more or less active function for a longer period. In such cases, the joints perform their functions under abnormal conditions, and, as a

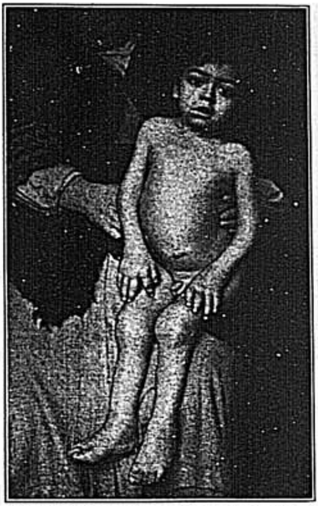

FIG. 3.—Symmetrical and general nodular swelling in a case of metabolic osteo-arthritis. The glands and spleen are enlarged and palpable. So-called Still's disease.

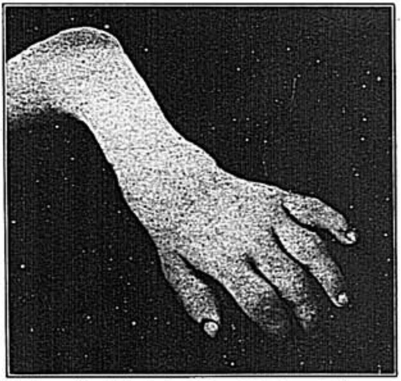

FIG. 4.—Nodular swelling of the hand and finger-joints in metabolic osteo-arthritis. In this case all the joints except those of the head and neck were involved. The liver, spleen, and glands were enlarged (Fig. 15).

consequence, the symptoms of joint irritation usher in the disease. The swelling then appears abruptly, is irregular or spindle-shaped, and, besides thickening of the soft parts, there is joint effusion. In this event, with the appearance of the swelling, there is loss of motion, pain, and deformity (in the hands the appearance is illustrated in Fig. 5). For this reason the joints are put at rest and the effusion then subsides to a certain extent, leaving the doughy spindle-shaped or nodular swelling behind. In the more energetic or in those who are compelled to work, depending upon the rapidity of the advance of the disease, this sequence may be repeated a number of times. It must, however, be remembered that the effusion is often very slowly absorbed, and in a fair number of cases remains permanently.

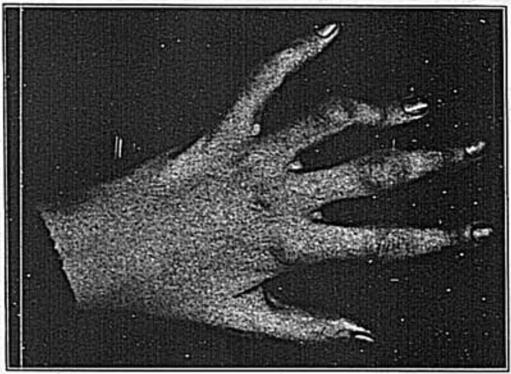

FIG. 5.—Flexion deformity with reactive effusion in metabolic osteo-arthritis. The effusion in this case almost completely disappeared when the joints were put at rest.

As joint effusion may occur from joint irritation, irrespective of the cause, it cannot, of course, be considered a characteristic symptom of any form of joint disease. Nor is nodular swelling an absolutely pathognomonic symptom of metabolic osteo-arthritis. In children it frequently involves all the joints of the extremities and remains present throughout the course of the disease (Fig. 2). But in adults, though it is nearly always present in the knees, it rarely involves the smaller joints of hands and toes. Moreover, certain forms of polyarticular infection with para-articular involvement which occur in children are characterized by a doughy nodular swelling of the joints. Such cases have frequently been mistaken for metabolic osteo-arthritis or have been considered analogous to it (rheumatoid arthritis,

arthritis deformans); and when, as sometimes happens, there are swollen glands, they have been described as Still's disease. This will be more fully dealt with later.

Joint Deformity. With the advent of the swelling, or soon after, muscular contraction, and with it joint deformity, makes its appearance. To the deformity the disease owes one of its most popular names. Virchow, I believe, first named it arthritis deformans. Following him, a great many Germans, and more recently some English writers (Garrod), call it so. Charcot, whilst he did not adopt the name, also considered the deformity one, if not the most, characteristic part of the condition. Indeed, he went so far as to divide the cases into types, according to the various forms of deformity which occur in the hands.

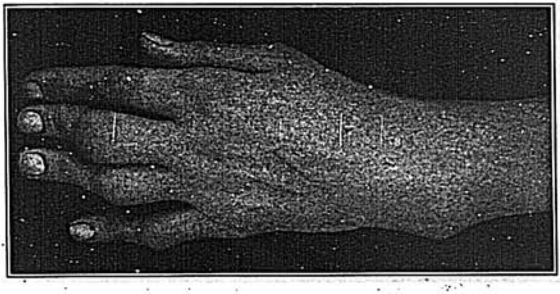

FIG. 6.—Palisade deformity in metabolic osteo-arthritis. There is no swelling.

The most characteristic deformities occur in the fingers. They are the so-called palisade deformity: flexion of the middle and extension of the terminal phalangeal joints (Fig. 6); deviation of the fingers to one side (Fig. 7); and flexion of the phalangeal, and phalangeal metacarpal joints (Fig. 1). Various forms of deformation may exist in the same patients in different joints, and combinations of any or all of them occur. In the larger joints the deformity differs in no wise from that which occurs in all other forms of joint disease. The knee is flexed and perhaps adducted; in the hip flexion and abduction are later succeeded by adduction and internal rotation.

Here, as in other joint diseases, the deformity depends upon two factors, viz., muscular contraction and tissue destruction. In the early stages deformity is due to muscular contraction alone, in the later stages to a combination of muscular contraction and bone destruction. In no other condition is this so well exemplified as in metabolic osteo-arthritis. In this condition, as well be shown later, rarefaction and softening of the articular ends of the bones precedes or is concomitant with the earliest joint symptoms. The softened bone not only gives way as the result of the pressure of muscular contraction and weight bearing, but later the location of the softening and absorption directly influences the extent and direction of the deformity. In the terminal stages of the disease, the articular ends of the smaller bones (fingers and toes) are more or less completely absorbed, and to this is due the striking deformity of the fingers. By means of a series of x-ray pictures the gradual evolution of the deformity may be graphically depicted.

Loss of Motion. Loss of motion depends upon a number of contingencies. In the early stages, as has been said, weakness is apt to be mistaken for stiffness, but later, when there is swelling and muscular contraction, there is, of course, real limitation of motion. In those cases in which the swelling remains nodular, contraction may be slight or transitory or entirely absent and passive motion may not be interfered with to any great extent. When muscular contraction is present, which sooner or later is the case, passive motion, unless there is mechanical joint irritation, is limited to the extent of the contraction, and the joint is quite freely movable within the limits of the contraction. So, for example, flexor contraction of the knee limits the motion in extension, but the knee may be still further flexed without difficulty. When, however, the contraction has existed indefinitely, and the joints are retained in one position for a long time, there is apt to be some further limitation of motion. Except during the transitory periods of joint irritation the limitation of

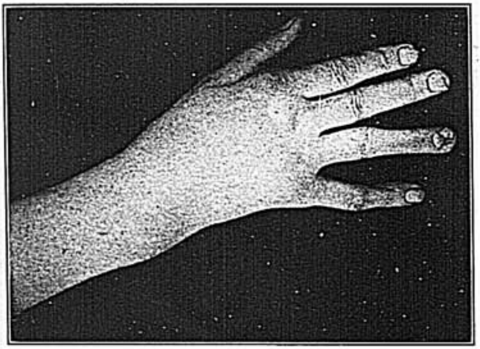

FIG. 7.—Lateral deviation of the fingers without swelling in metabolic osteo-arthritis.

motion is never absolute, nor does it keep pace with the progress of the disease; for patients with extensive disease and much deformity often have a considerable range of passive motion.

Though some of the joint symptoms are peculiar and often very characteristic, it is evident that in metabolic osteo-arthritis, just as in other joint diseases, it is harzardous or impossible to make a positive diagnosis upon the intrinsic joint symptoms alone. Owing to their superficial situation and their peculiar functions (motion and weight bearing), the joints themselves present essentially the same intrinsic symptoms in all forms of disease. Thus, pain, swelling, muscular spasm with its attendant deformity, and loss of passive or active motion appear as symptoms of not only all forms of joint disease, but, indeed, may be induced by joint irritation caused by an abnormality near, but not directly involving the joint at all.

Hence, though advanced cases of metabolic osteo-arthritis present such a peculiar and characteristic deformation of the fingers that the diagnosis can be made from it without any difficulty, these symptoms are not so definite in the other joints and are not present at all in the early stages of the disease. Nodular swelling, characteristic as it is, is not pathognomonic; for such a swelling may appear in any condition with peri-articular infiltration and thickening. Pain is all extremely variable symptom. Muscular contraction is present in an joint diseases and deformity is dependent altogether upon mechanical conditions. We are here, as elsewhere, therefore, compelled to depend upon the influence which the character of the morbid process exerts upon the onset, course, and termination of the joint condition and upon the actual condition in the joint as shown by the radiograph, for the diagnosis. In metabolic osteo-arthritis this influence is definite and characteristic.

Onset and Course. The condition is always polyarticular and symmetrical. It always attacks the peripheral joints first and a number of joints are usually affected simultaneously. The onset is invariably insidious. There is no foundation for the division into acute, subacute, and chronic cases, advocated by Garrod. This classification, which is based upon the abrupt onset of the swelling, has led to the confusion of this joint condition with certain forms of polyarticular infection with which it has absolutely no connection. The abrupt onset of the joint swelling is due, as has been already explained, to mechanical irritation, and careful (not suggestive) inquiry will always elicit symptoms which have preceded the swelling. In a large percentage of the cases the disease comes on so insidiously that the patient is unable to state definitely just when the trouble began.

Not only is the onset insidious, but in cases uncomplicated by joint irritation the course is gradually progressive. In some cases, it is true, the disease progresses more rapidly than in others, but even in the most rapidly destructive forms the disease advances gradually, and there is never a really abrupt onset and acute local and general reaction. In the majority of cases the disease progresses slowly and very gradually. Preceded by more or less decided subjective symptoms, a number of joints become weak or stiff. With increasing weakness or stiffness joint swelling appears; hardly perceptible at first, when uncomplicated by mechanical joint irritation, it gradually increases, becomes spindle-shaped, and then perhaps nodular. In many cases the nodular appearance of the swelling is due to the extreme atrophy of the peri-articular structures and not to thickening of the joint membranes or bones. Thus it remains for a variable length of time, when it just as gradually recedes, finally disappears altogether, leaving the joints atrophied and deformed. The deformity, in its turn, increases by degrees, and though passive motion may not be markedly limited, it gradually and progressively leads to crippling. In the meantime new joints become involved in the same insidious and progressive manner, and in the severer cases, beginning in the periphery and proceeding toward the trunk, all the joints, including those of the spine, may become involved. Though there are never intermissions, even in severe cases, there are times when the disease progresses less rapidly or remains stationary for a variable length of time. The periods of apparent quiescence may, indeed, continue for several years; but in the severer forms the condition ultimately resumes its relentless course and the individual finally becomes a helpless cripple.

In the milder cases the disease progresses very slowly, with long periods of quiescence and less extensive crippling. In some cases, indeed, the disease, after progressing to a certain extent, seems to remain stationary, and though the affected joints remain crippled, no more joints become involved. It is, however, very difficult to say definitely that the disease will make no further progress in a given instance; for it not infrequently again becomes active and progressive after years of quiescence.

Differential Diagnosis. With one exception (polyarticular form of senile osteo-arthritis, Heberden's nodes) there is no other chronic polyarticular joint condition in which the joints are symmetrically and progressively involved. In children the condition, because of the absence of joint irritation (they are not compelled to use the joints in spite of pain and disability, as adults often are), occurs in its purest form. In them the nodular swelling, which comes on very gradually, remaining present for a very long time, with slight or no loss of passive motion, is so characteristic that it is quite impossible to mistake it for any other joint abnormality. In adults, however, the inexperienced observer may occasionally find difficulty in making the diagnosis. This is most apt to be the case when the disease comes on very insidiously and progresses very gradually. In such cases the prodromal symptoms, being slight, may be overlooked and the frequently recurring symptoms of joint irritation might lead one to believe there are recurrent attacks with an abrupt onset. Under these circumstances the slight rise in temperature which is occasionally present has led many otherwise good observers to believe that the malady is infectious. But if it is remembered that the polyarticular joint infections are always due to a general infection (sepsis), that the onset is very acute, with marked constitutional symptoms and rapid but not progressive joint involvement, this mistake in the diagnosis is readily avoided. What has caused most confusion in regard to the differentiation of these conditions are the cases of infectious polyarticular joint disease seen long after the initial disease has subsided. In these, if the history is not obtained, the deformed and stiff joints of the hands may lead the surgeon to believe he has a chronic joint disease to deal with. Indeed, these cases are nearly always mistaken for cases of metabolic osteo-arthritis, and called rheumatoid arthritis, or arthritis deformans. This is unfortunate, for in cases of polyarticular infections we are not dealing with an active joint disease at all, after the acute attack has once subsided, but simply with the deformity and stiffness; that is, the result of the disease. A history of the case, that is, sudden onset with high temperature and symptoms of profound intoxication, which may or may

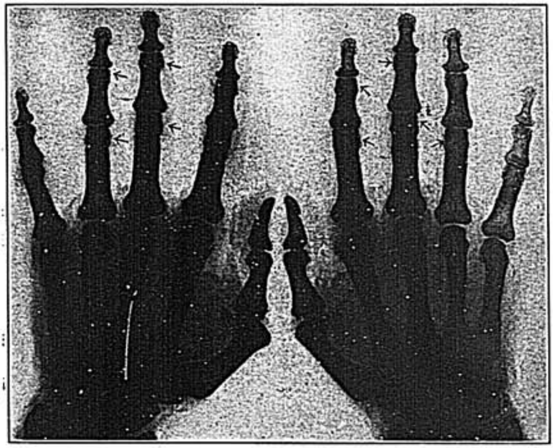

FIG. 8.—Radiogram showing the condition of the bones in a very early stage of metabolic osteo-arthritis. This picture is taken from a radiogram of the hands shown in Fig. 2. The arrows point to the rarefied areas. (Radiograms to show these changes must be properly exposed and developed very carefully.)

not have been recurrent, are diagnostic of the polyarticular infections and readily distinguishes them from metabolic osteo-arthritis. If for some reason the history is not obtainable, the fact that the joint lesions are not progressive and that the joints are always ankylosed (bony) when the bones are involved, and show no bone changes at all when the bones are free, readily clears up the diagnosis.

When cases cannot be observed for any length of time, or when for some reason the diagnosis is doubtful, the x-rays will always definitely decide it. Good radiograms, particularly of the small joints of the extremity, show very characteristic pictures in the earliest stages of the the disease. Even before there is deformity, a characteristic rarefaction of the bones can be easily made out. At this time, the rarefaction is confined to small circumscribed areas in the epiphysis just below the cartilage (Fig. 8). As the disease advances these areas are found to become gradually larger (Figs. 9 and 10) (more and more bone becoming absorbed), and in the case of the smaller joints the epiphysis, as a whole, may finally disappear. This peculiar form

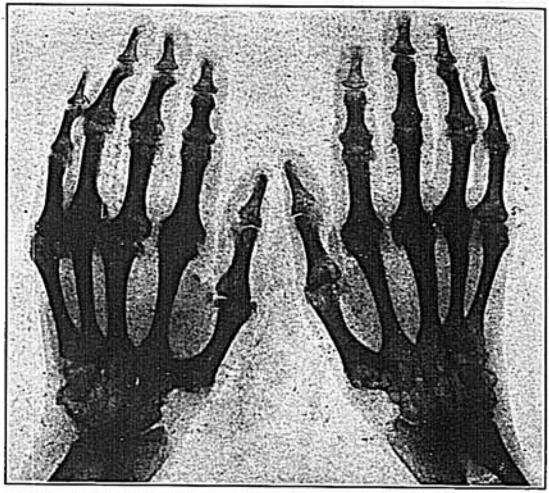

FIG. 9.—Radiogram of the hands in a more advanced stage of metabolic osteo-arthritis than is shown in Fig. 8. The rarefication has spread, some of the epiphyses are distorted, and some of the joints are subluxated. The pressing together of the softened carpal bones gives the appearance of bony ankylosis; but there is no ankylosis, for the joints can be moved passively.

of rarefication differs radically from that shown by x-ray pictures in the polyarticular forms of infectious osteo-arthritis. In the latter it is diffuse from the beginning, not infrequently involving the shaft (Fig. 11). When recovery is not complete in the later stages it is always accompanied by periosteal outgrowth and bony ankylosis (Fig. 12). In the early stages of the other forms of trophic osteo-arthritis (senile and neurotic osteo-arthritis) the same form of rarefication occurs; but as these forms of joint disease practically always involve the larger joints, the changes are not so readily made out. The senile and neurotic forms of osteo-arthritis are easily differentiated from metabolic osteo-arthritis by the presence of periosteal outgrowths of various kinds, the so-called hypertrophic processes. As a result of the softening of the bones in metabolic osteo-arthritis, the articular ends of the bonds, particularly of the large joints of the lower extremity, become distorted in the later stages of the disease. This is, of course, readily made out in the x-rays. At times the softened bones spread as the result of weight bearing, and occasionally, particularly in the knee, the thin edges of the articular surface turn over. These lips have been mistaken for periosteal or cartilaginous outgrowths, in the interpretation of the x-ray picutres, by some observers. Careful observation in conjunction with the examination of pictures of other joints will prevent such an error.

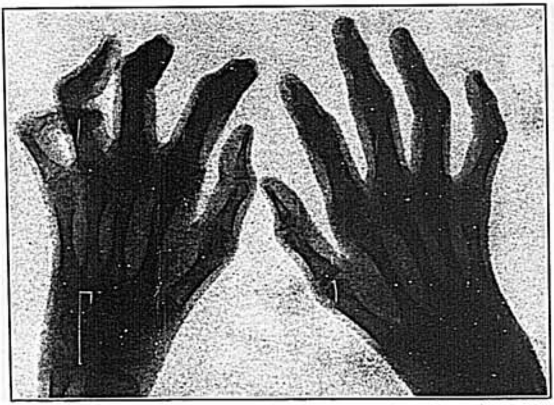

FIG. 10.—Radiogram of the hands shown in Fig. 1, an advanced case of metabolic osteo-arthritis in a child, with extreme rarefication. All the joints can be passively moved. Here as in all cases of metabolic osteo-arthritis there is no proliferation or hypertrophy.

If we combine the characteristic clinical phenomena with the *x*-ray findings in metabolic osteo-arthritis, we have a symptom complex which is pathognomonic. Hence, if a given case of joint disease is polyarticular, involving the peripheral joint first, with a marked tendency to be symmetrical, if the course of the disease is gradually progressive, new joints being involved from time to time; if the physical joint changes begin with swelling which is followed by gradually increasing deformity; and if the radiograms show the peculiar punched-out rarefication in the early stages, and the absorption and distortion in the late stages, without the presence of proliferative processes or bony ankylosis, no matter what other condition may be present, it is absolutely certain that the joint disease is metabolic osteo-arthritis. And only when this combination of symptoms is present are we dealing with this condition.

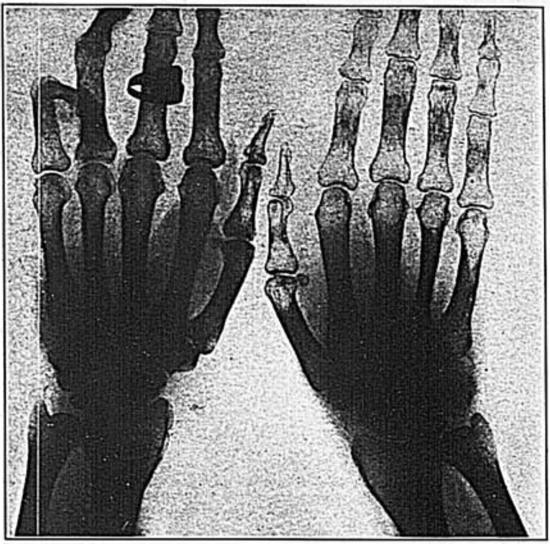

FIG. 11.—Radiogram of the hands in infectious osteo-arthritis, showing the tendency of the rarefication to involve the shaft immediately. The left hand was first affected, and the disease, which had here run its course, has lead to bony ankylosis in the fourth and fifth fingers.

As time goes on, and we become more familiar with the scientific differentiation of joint disease, there is no reason why, with such striking clinical phenomena, the diagnosis should not be made without the aid of the x-rays.

PATHOLOGY. As was said in the beginning, the main cause for the misconceptions which prevail regarding the chronic joint diseases is, that the pathology has not been studied in conjunction with clinical observation. With one exception (Kachel[1]) pathological findings have been described as derived from cases of arthritis deformans or rheumatoid arthritis, without an adequate, or, in some instances, without even a hint of the clinical history of the case. Hence, as the ideas of what was arthritis deformans or rheumatoid arthritis differed, and as the pathological specimens were often obtained from totally different conditions, it was only to be expected that misconception should ensue.

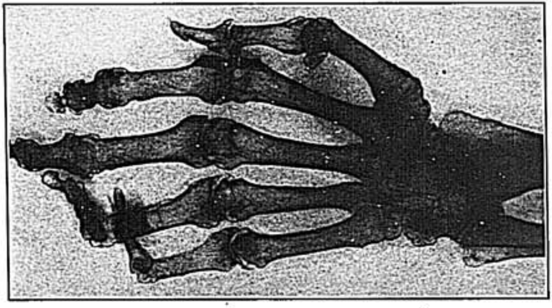

FIG. 12.—Radiogram of the hands of a case of polyarticular infectious osteo-arthritis, which ran its course many years ago. Bony ankylosis and diffuse rarefication of the shaft have occurred.

In the present instance particular care was taken to study the pathology only in such cases in which the clinical diagnosis was unmistakable and corresponded to the symptom complex here designated as characteristic. The pathological study here presented is based upon six cases which came to autopsy. About thirty joints were carefully examined, both macroscopically and microscopically. Besides the cases in which there was a complete autopsy, I have examined individual joints, ten in number, from various sources in which the clinical diagnosis was positive.

In the majority of instances the description of the pathology of metabolic osteo-arthritis begins with a description of the changes in the synovial membrane or the cartilage, and I believe nearly all authorities are of the opinion that the disease begins in one or the other of these structures. Under these circumstances, one who studies the pathology of metabolic osteo-arthritis is surprised to find the cartilage quite normal and the capsule with insignificant changes during the early stages of the disease. Upon opening a joint which had shown distinct abnormality during life (swelling, pain, deformity), one often finds little besides capsular irritation and a small amount of effusion in the interior. At this stage, though the cartilage is apparently quite normal, the articular ends of the bones, particularly those of the larger joints of the lower extremity, often show considerable distortion. Moreover, if the epiphyses are cut into or sawn, it is found that they are decidedly softer than normal; and if the disease is at all advanced, they may be cut readily with a scalpel.

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[1] Untersuchungen über Polyarthritis Adhesiva, Ziegler's Beiträge, Band xxxiii.

If a section of the articular end of the bone is examined, one finds the marrow more red, and the trabeculæ of the spongiosa diminished in number and thinner than normal. During the early stages the bone atrophy is distinctly subchondral, but it gradually advances and finally involves the whole epiphysis. In a majority of cases at an early stage, one can discover with the naked eye, or at any rate with a low-power magnifying glass, minute cavities situated in the subchondral region of the epiphysis within, or at the edges of the bone trabeculæ. These are bone cysts and they vary in size, being of course larger and more numerous as the diseases advances. The more recent ones are apparently filled with a mucilaginous material; the older ones are empty. Besides the cysts there are in the subchondral and later in the deeper portions of the epiphysis as well, opaque areas resembling foci. These focal areas are composed of more or less dense connective tissue. In the later stages these areas of connective tissue have increased considerably, and frequently have coalesced to form extensive areas. In the terminal stage the connective tissue not only invades the deeper portions of the epiphysis, but when the cartilage has in part, or, as a whole, disappeared (which is usually the case), it also invades the interior of the joint.

As has been said the cartilage shows no changes during the early stages of the disease. Indeed, in joints which, because of muscular contraction have been held stiff for a long time, it may be covered to some extent by connective tissue, without showing marked signs of degeneration or ulceration. In such cases the connective tissue is not derived from the cartilage by splitting and fibrillation as the previous writers upon this subject suppose, but can be traced to the zone of capsular insertion from which it originates. It exactly resembles the connective tissue (loosely vascular), which appears in all joints that have been immobilized (without bony ankylosis) for a long time. And I have convinced myself that in cases of metabolic osteo-arthritis, in which it is present before the cartilage has been affected, it is due to the immobilization and is not a part of the pathological process. That it is not part of a proliferative process which beigns in the capsule is evident from the fact that it is frequently present when the capsule shows no signs of proliferation anywhere else. (It is then exactly analogous to the connective tissue which is found between the joint surfaces in the normal joints of animals which have been immobilized for experimental purposes. In such cases the joint motion is found limited when the retention dressing is removed; this limitation of motion is found to be due to muscular contraction just as in metabolic osteo-arthritis; similarly when the tendons are cut free motion is again possible. In the interior of the joints the cartilage is found covered with a layer of loose, somewhat vascular, connective tissue which exactly resembles that described above).

As the disease advances the subchondral changes increase, and the nutrition of the cartilage being impaired it becomes involved in the pathological process. It loses its lustre, splits, ulcerates, and finally disappears altogether. In the joint disease under discussion, whatever may be the case elsewhere, the joint cartilage never shows any signs of proliferation. It is true that at an early stage, on microscopic examination, one occasionally finds cell multiplication to a limited extent, but here, at any rate, the cellular increase is simply a prelude to degeneration, and there is never an increase in the amount of the cartilage to be made out macroscopically. The chondromas which are described as occurring in arthritis deformans (which by the way are not chondromas at all, but consist of uncalcified osteoid tissue derived from the periosteum) do not occur in metabolic osteo-arthritis. Nor are periosteal outgrowths of any kind ever to be found.

The degeneration of the cartilage varies according to the location and extent of the disease in the underlying bone. At times it appears focal, but close examination will always reveal changes extending some distance from the supposed focus. Naturally, degenerated or degenerating cartilage loses its functional power and hence suffers from pressure. For this reason the so-called cartilaginous ulcer appears where the articulating surfaces are held firmly together by muscular contraction. As soon as a defect occurs it becomes filled with connective tissue. This connective tissue, which comes from the degenerating spongiosa, soon fills up the gap in the cartilage and invades the interior of the joint, where it comes in contact and coalesces with the connective tissue derived from the border of the capsule. In this wise the joint cavity becomes more or less completely filled with connective tissue; and if the cartilage degenerates completely (the usual condition in the terminal stages of the disease), the articular surfaces of the opposing bones are separated, or, more correctly, united by connective tissue. This new-formed connective tissue is not dense, but loose and vascular. There are few round cells within it, and none in the neighborhood. It does not involve the capsule, which indeed may be rudimentary. It shows no marked tendency to contraction, so that it does not cause ankylosis or even marked joint stiffness. When there is limitation of motion in these cases, it is due to muscular contraction and disappears when the tendons are cut.

The capsular changes, supposed by many to be the earliest, are really insignificant. In the joints in which the disease is just beginning, there is simply a small amount of effusion and some injection. At times there is some hypertrophy of the synovial fringes—but as far as my own cases go, there is never the enormous villous formation described by some authors. Later, the capsule degenerates with the other parts of the joint. It becomes lax, more succulent; the inner surface loses its lustre; the synovial fringes which may have been somewhat hypertrophied during the earlier stages undergo fatty degeneration; and, finally, only a few shreds of degenerated capsule mark its former location.

Thus, macroscopically, the disease manifests itself by a degeneration and gradual disappearance of the joint structures. The bone ends, which in the early stages are distorted and deformed, in the later stages become rudimentary, and in the small joints disappear entirely. The rarefication and bone absorption are best demonstrated in the dried specimen. Thus, Fig. 13 represents the femur of an advanced stage of metabolic osteo-arthritis. The femoral head is rudimentary, and the bony tissue is so thin and delicate that it breaks like eggshell between the fingers. Fig. 14 shows a cross-section of the head of the femur in another less advanced case, showing distortion, rarefication, and cyst formation. Unlike the cases of monarticular trophic osteo-arthritis, in which the articular ends of the bones are also somewhat rarefied and softened, there are never signs of proliferation (pseudohypertrophic processes) in metabolic osteo-arthritis.

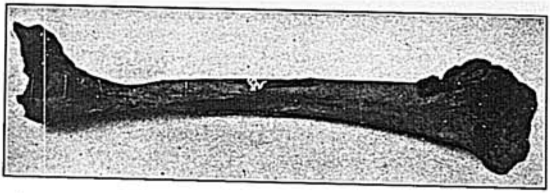

FIG. 13.—Femur from a case of metabolic osteo-arthritis. The head of the femur is almost entirely absorbed; both epiphyses are extremely delicate and break between the fingers like eggshell.

In the terminal stages of the severe cases the small joints almost completely disappear. The opposing articular surfaces are separated by connective tissue, there is no joint cartilage, no joint cavity, and the capsule, ligaments, and even the tendons in the neighborhood are reduced to mere shreds.

Microscopic Examination. Osteomalic and osteoporotic changes are present side by side, and they differ in nowise from those found in other forms of bone degeneration. There can be no question regarding the softening, for on staining with hematoxylin and carmine certain areas of what should be calcified bone, and, therefore, take the carmine stain, are colored blue (hematoxylin) instead. In such areas the bone-cell cavities are larger than normal. The cells show various degenerative changes. At times they are larger than normal, but take the stain with difficulty; later they are shrivelled, the processes are absent, and finally they completely disappear.

The ground substance becomes cloudy and granular. The bone-cell cavities increase in size, a number of them coalescing to form larger cavities filled with a mucilaginous fluid, thus forming the cysts. As the process advances, the bone cysts increase in size, more and more of the softened bone substance being absorbed; thus the trabeculæ become much reduced in thickness, and finally many of them completely disappear. Lacunar absorption also occurs, and Howslip's lacunæ are to be seen upon the surfaces of the trabeculæ.

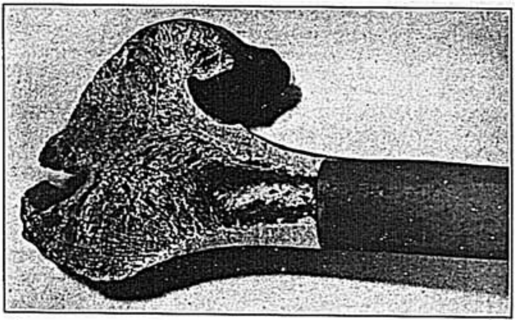

FIG. 14.—Section of the head of the femur, showing the distorsion and the rarefication.

The marrow shows marked signs of degeneration. The fat is diminished, and in the earlier stages is displaced by a mucin-like fluid. Later the connective tissue fills the spaces between the degenerating trabeculæ. In a like manner connective tissue fills the cysts forming the opaque areas seen with the naked eye, and finally, after the disappearance of the cartilage, it penetrates the interior of the joint.

The changes in the cartilage are those which occur in all forms of degeneration in this structure. Proliferating cells occur in the early stage, but these are comparatively few in number and no doubt simply usher in the degenerative process. The cells assume various abnormal shapes, are stained with difficulty, and ultimately disappear altogether. The cell cavities enlarge, the ground substance loses its hyaline character, becomes granular or fibrillated, and ultimately splits and loses its connection with the bone. In those situations where there is pressure, at times also in other places, the articular ends of the bones become denuded in somewhat circumscribed areas, the so-called ulceration of the cartilage. Such defects in the cartilage become filled in with the connective tissue from the bone below, and and to a lesser extent with that which comes from the border zone of the capsule. These defects or ulcers are not caused by the active invasion of the connective tissue from the interior of the joint into previously healthy cartilage, as described by many writers. This is improbable in any case, because normal cartilage cannot for physiological reasons be invaded by connective tissue. In the present instance there is evidence besides, in direct contradiction to such a method of invasion. In the first place, the bone changes are found to be present both macroscopically and microscopically before the cartilage or capsular changes. In the earlier stages of the disease the capsule and cartilage are not involved, whilst the bone degeneration can be readily demonstrated, if not with the naked eye, certainly with the microscope. If the process is carefully followed it is found that the cartilage begins to degenerate at a stage when the amount of connective tissue, particularly that in the interior of the joint, is insignificant. And, finally, if a number of joints are examined, one is sure to find defects in the cartilage which have not as yet become filled with connective tissue. In the majority of instances, the connective tissue in the ulcers can be directly traced to the bone, and as the joint interior only becomes quite filled with connective tissue in the terminal stages of the disease, considering the nature of the process generally, it seems to me only plausible to assume that it originates within the epiphysis.

The capsule shows no characteristic changes. I have never been able to find the enormous proliferation of the villi spoken of by some authors. I am fully in accord with Shuchardt in this respect. Aside from a slight sign of irritation in the early stages, there is a gradual atrophy of the capsule and ligaments, with or without some indication of fatty degeneration.

Thus the joints in metabolic osteo-arthritis present pathological changes which correspond and readily explain the clinical phenomena. The earliest changes are bone changes, and these early bone changes can readily be demonstrated by x-rays during life. The rarefication which is shown by the radiograph to be subchondral and somewhat circumscribed (punched-out rarefication) in the early stages, corresponds to the osteomalic and cyst-like osteoporotic condition to be seen in the postmortem specimens. Proliferation processes are never seen during life, and they are never found when the joints are examined after death.

The clinical phenomena indicate that the condition is one of gradual joint degeneration, and the postmortem findings readily bear this out. As a matter of fact, the condition presents a pure form of atrophic degeneration, as was indicated by Shuchardt when he classed this condition as an atrophic joint inflammation. That it is not an inflammation, however, is evident from both the symptoms during life and the pathological changes in the joints.

In metabolic osteo-arthritis we have, then, a perfectly distinct joint condition which can be distinguished from all other joint conditions both clinically and pathologically. Having decided this point, we are in position to inquire whether this joint condition is of itself a disease, secondary to some other disease, or a part of a distinct general condition. Having constantly in mind that whatever the concomitant phenomena, to be spoken of presently, the joint condition in every case remains exactly the same and corresponds in its diagnostic and pathological features to those here detailed as characteristic of metabolic osteo-arthritis, we proceed to the discussion of—

THE GENERAL OR CONSTITUTIONAL SYMPTOMS PRESENT IN PATIENTS WITH SUCH A JOINT CONDITION. A fairly large percentage of cases shows no definite general abnormality of any kind, except a variable degree of cachexia and secondary anemia throughout the course of the disease. In the milder cases the anemia and emaciation are not very marked, and increase very slowly. In such cases the internal organs show no clinical signs of abnormality whatever. The joint condition progresses slowly and gradually for a number of years, may remit occasionally or become quiescent, and after a variable amount of crippling the patient finally succumbs to some intercurrent malady. In the severest forms, the joint condition progresses rapidly and the cachexia, emaciation, etc., become extreme; and when the external conditions are unfavorable the individual, after a few years of suffering, becomes marantic and dies. Between the mild and the extreme cases there are all grades. In another class of cases, there is a slight rise in temperature in the beginning which remains, with slight remission, continuous for a long time. In these cases the joint condition differs in nowise from that in the cases without fever, and the joint disease continues to progress in the afebrile stage. This, aside from the fact that the joint disease begins insidiously, readily differentiates these cases from the polyarticular infection in which the progress of the joint condition always subsides with the subsidence of the temperature and constitutional disturbance.

Increased pluse rate, even tachycardia, is not an uncommon symptom in both the febrile and the afebrile cases. It is sometimes severe enough to be apparent to the patient, who then complains of palpitation. Such individuals are apt to be, but not necessarily, troubled with symptoms of functional nerve derangement. In some there is only slight nervousness, but in others there is marked irritableness, abnormal anxiousness, and insomnia. But nervous irritability and functional nervous troubles generally are not particularly characteristic of those with increased pulse rate; such symptoms are common in metabolic osteo-arthritis without tachycardia. That intelligent people who are helplessly crippled should become hypochondrical is not surprising, and does not imply, as some observers would have it, a definite derangement of the higher nerve centres.

Muscular atrophy of a more or less general nature is a marked and constant symptom in osteo-arthritis. To a large extent it can be ascribed to the general emaciation and the causes, whatever they may be, which usually cause this condition in other joint diseases. But in many cases it is so extreme and manifests itself by weakness so early (even before there are perceptible changes in the joints), that it seems not unlikely that other factors besides are influential in its production. In nearly all cases the reflexes are exaggerated. This is to be expected along with other functional nervous derangements. Of a much more specific character is fibrillar contraction which occurs in many cases. This symptom is present when the disease is well advanced, and manifests itself when the muscles are at rest and in action.

According to numerous French observers skin lesions are common in patients suffering from metabolic osteo-arthritis. But from my own observations, which are in accord with those of Pribrim, I have not, with one exception, found them more frequent than one could expect in otherwise normal individuals. Trophic conditions of the nails are occasionally present, but they are not distinct or frequent enough to be considered characteristic. Glossy skin, spoken of by some authors as a characteristic symptom, must be rare, for I have not seen it once in an undoubted case of metabolic osteo-arthritis. On the other hand, I have seen it several times in severe polyarticular infectious osteo-arthritis, and for this reason I think many if not all the cases reported must be based upon a faulty diagnosis. The same seems to be true of the so-called rheumatic nodes. In none of the cases of joint disease I have seen, in which nodes were present, was the joint condition metabolic osteo-arthritis.

Œdema and even scleroderma have been reported. The scleroderma I have not seen; it must be a rare condition, but in a number of cases œdema was present. In these instances I have had the impression that the œdema which occurs in patients without cardiac or kidney lesions, was similar if not analogous to that which occurs in certain neuroses.

A very peculiar and interesting condition of the fingers occasionally presents itself in these patients. The abnormality appears to be due to some change in the skin, and for this reason is discussed under this heading; but in reality it is due to atrophy of the bones and subcutaneous tissues, the skin remaining intact. In consequence the skin hangs loosely over the fingers, and in severe cases the effect of a worn glove is strikingly reproduced. Some authors have considered this condition to be due to an œdema which, after stretching the skin, has disappeared; but as I have known it to occur in cases in which no œdema had been present, for this as well as other obvious reasons, this explanation is more than improbable. Moreover, in just such cases the extreme atrophy of the bone can be demonstrated by the *x*-ray pictures.

Since the theory of uric-acid intoxication has been abandoned, there remains little to be said regarding the condition of the urine in cases of metabolic osteo-arthritis. So far nothing characteristically abnormal has been found. In the terminal stage of the disease, in children, albumin is present in some cases. It is absent in the majority of the cases, however, and its relation to the condition, if there is one, has not been ascertained.

In children, metabolic osteo-arthritis occurs in connection with two apparently distinct constitutional conditions. One exactly corresponds with that of the afebrile type in adults. The other is a very characteristic condition which, with some evidently different conditions, is known as Still's disease. In 1897 Still described what he considered a characteristic joint disease of early childhood, which manifested itself by the gradual onset of more of less symmetrical joint swelling, enlargement of the glands and the spleen, and fever. According to Still, the disease is progressive and gradually involves all the joints of the body. Since then, all cases of polyarticular joint swelling with fever and glandular enlargement have been designated Still's disease. Now, as has been indicated, certain forms of polyarticular infection in children are characterized by polyarticular nodular swelling, which may or may not be symmetrical. In these cases there is often glandular swelling, and sometimes the spleen is also enlarged and palpable. These cases are usually called Still's disease. Whether it is proper to call them so remains for Still to say, for he considers the condition that bears his name infectious.

It is certain, however, that these cases differ radically from a definite condition occurring in children, in which the joint disease, whatever the general condition, is certainly not infectious. I have seen ten such cases with two autopsies. The joint changes are purely degenerative and correspond exactly with those of adult forms of metabolic osteo-arthritis. Of course, owing to the preponderance of the cartilage in young children, the bone changes are not so definite and cannot be made out in radiograms.

The disease comes on insidiously, symmetrically involves the peripheral joints first, thence gradually procedes to those of the trunk, and finally all the joints of the body become affected. In these cases there is very little or no pain, and the children rarely complain of it, unless compelled to walk or are roughly handled. There is moderate but general glandular enlargements. Not only the glands in the neighborhood of the affected joints are involved, but all the glands take part in the process; and at autopsy I have found decided swelling of the bronchial and mesenteric glands. The spleen is invariably enlarged and palpable. At times the liver is also enlarged, and in some cases extends far down below the free border of the ribs. (Fig. 15 shows a child in whom the liver and spleen are so large that although there is no ascites, the abdomen is markedly protuberant.) There is a moderate continuous temperature, with secondary anemia and cachexia.

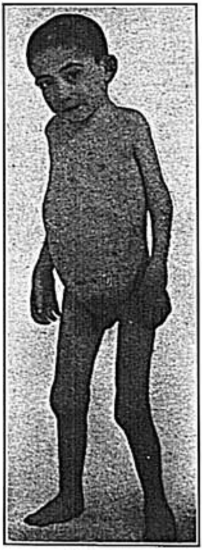

FIG. 15.—Case of metabolic osteo-arthritis in a boy. (The hand is shown in Fig. 4.) The liver and spleen are so large that they cause marked protuberance of the abdomen.

Whether Still includes cases of this nature with the polyarticular infections, I cannot quite make out. In the conditions I have outlined above, the fingers were always involved; this does not seem to be so in the cases reported by Still and others.

From the study of the general symptoms, it is evident, that while the joint condition remains uniform, the constitutional symptoms vary within wide limits. It is quite improbable that a primary uniform joint disease should be responsible for such variable general symptoms, much less such totally distinct constitutional conditions as, for instance, the two forms which occur in children. We may, then, without resorting to further argument, conclude that the joint disease is not a primary local condition causing secondary general symptoms. The next question to decide is, Is the joint condition secondary to some specific general abnormality. That there is some morbid condition which affects the metabolic processes is evident; the cachexia, the effect upon the nervous system, upon the heart (tachycardia), and even upon the vascular system (for vasomotor disturbances have been observed in a number of cases), the symmetrical and progressive character of the joint lesions all speak for this. However, although it cannot be denied that some metabolic disturbance is responsible for the joint and some of the other symptoms, this does not necessarily prove we are dealing with a uniform and specific general disease as a cause.

On the contrary, the variability of the general symptoms plainly indicate that this cannot be the case. Indeed the fact that perfectly typical cases of metabolic osteo-arthritis are known to occur in the course of widely differing diseases, plainly indicates that the constitutional condition, whatever its relation to the joint condition, may owe its presence to totally distinct and opposite morbid influences.

Whatever may be the case with the other skin diseases, it is certain that individuals who suffer from psoriasis show a marked tendency to have trophic joint disease. And although the lesions in such cases are not always typical metabolic osteo-arthritis, so many of them are that we must conclude, as was suggested in one of my previous papers, that the two conditions are in some way related. Their relation to each other or to the common cause need not again be discussed. That the pathogenesis and cause in cases of metabolic osteo-arthritis with psoriasis is different from that of metabolic osteo-arthritis without this skin lesion seems a reasonable conclusion. For it is quite unlikely that a given pathogenic factor should directly produce such a typical skin lesion in one case, and be present in another without causing such lesions.

Basedow's disease is another distinct disease in the course of which metabolic osteo-arthritis may develop. In this instance the relation to metabolic osteo-arthritis has been erroneously interpreted in a number of cases reported. So-called rheumatoid arthritis and Basedow's disease have been thought to co-exist, when, as a matter of fact, the Basedow followed a general infection with joint symptoms (infectious polyarthritis or osteo-arthritis). What I refer to here, however, are typical cases of metabolic osteo-arthritis, which come on in more or less typical examples of exophthalmic goitre. I have seen two such cases. In a third case, besides the typical joint disease, there were exophthalmos, large liver, spleen, and glands, with tachycardia. A similar case has been reported by Dr. Manges.[2]

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[2] Mt. Sinai Hospital Reports, vol. i.

That tachycardia and nervous symptoms occur in connection with metabolic osteo-arthritis was, I believe, first pointed out by Spener; and the similarity of these symptoms with those of Basedow's disease has since been suggested by a number of authors. Besides a number of cases with typical Basedow and typical metabolic osteo-arthritis have been reported. Here, again, the constitutional symptoms vary greatly. From the cases previously referred to, in which there is simply increased pulse rate, to the cases with distinct tachycardia, exophthalmos, large thyroid (typical Basedow's), there are various grades of constitutional disturbance suggesting this condition.

Still more striking, however, is the fact that typical metabolic osteo-arthritis may occur in the course, and apparently as the result of pulmonary tuberculosis: not that the conditions generally spoken of as tuberculous rheumatism are always cases of this joint disease, for all forms of joint disease due to direct infection, acute toxemia, and trophic conditions have been so designated. As far as trophic or degenerative conditions of the bones and joints are concerned, three distinct forms occur with pulmonary tuberculosis; these are: (1) Monarticular forms of trophic osteo-arthritis (senile type). (2) Hyperplastic peri-ostitis or ostitis (osteo-arthropathie hypertrophiante pneumique, Marie) (so-called club fingers). (3) Metabolic osteo-arthritis. That so many diverse conditions should occur under these circumstances, is not surprising when it is considered that the tubercle bacilli secrete no toxin, but cause toxemia or general disturbance because of the disintegration of the tubercle bacilli themselves. As the tubercle bacilli are complex bodies, it is to be expected that their disintegration and absorption should cause variable symptoms and conditions.

It is plain, then, that metabolic osteo-arthritis occurs not only in individuals who present variable constitutional symptoms, and, therefore, no doubt have variable constitutional abnormalities, but it also occurs in the course, or as the result of totally distinct and well-recognized diseases. Hence it cannot be due to a distinct and uniform general disease.

Nor to judge from the totally distinct character of the morbid conditions with which it is associated, can it be due directly to the various causes which induce these conditions. For it is quite unreasonable to suppose that a morbid condition like that due to the tubercle bacillus, which either causes changes due to direct invasion or to a toxemia, which necessarily involves some irritation (degeneration with proliferation, or even inflammation), should in certain isolated examples induce such a purely atrophic degeneration as occurs in metabolic osteo-arthritis; still less so, that such a pathogenic factor should directly induce the same pathological changes, as do others so totally different, as those which are responsible for the other conditions with which metabolic osteo-arthritis is known to be associated.

The only reasonable supposition is that all these conditions are active in producing an analogous general disturbance of the organism which in turn causes the joint degeneration. Indeed, it has been suggested that a general nervous derangement is the cause of it. But this cannot be true, because derangements of the nervous system, diseases of the spinal cord or the brain, or peripheral nerve lesions do not cause conditions like metabolic osteo-arthritis, but others, such as trophic osteo-arthritis of the senile type.

On the other hand, differing as they do in their origin and nature, the conditions, known or unknown, with which metabolic osteo-arthritis is associated, all have one thing in common. This is their deleterious influence upon the general nutrition. It matters little in what way this influence is exerted, as far as the tissues are concerned; upon them the result is the same, viz., inadequacy of the nutrition. In metabolic osteo-arthritis, the joint condition, a pure atrophic degeneration, exactly corresponds to what one would expect under such circumstances.

As a matter of fact, if we can rely at all upon the principle of general pathology, the changes which are typical of this condition could only be caused by a purely nutritive anomaly. Hence the conclusion that metabolic osteo-arthritis is due to a metabolic derangement which seriously impairs the joint nutrition is inevitable.

Whether or not the vice of the metabolism is of a peculiar kind, it is impossible, in the present state of our knowledge, to say. It is certain, however, that no toxic substance in the circulation can directly cause the joint changes. If a toxemia or auto-intoxication is present, its toxic effect is not exerted upon the joints directly, but indirectly through the impaired nutrition. All the toxemias, acute and chronic, with which we are familiar, when they act directly, induce similar changes in the bones or joints. When they act acutely they cause acute inflammation; when chronic they cause hyperplastic periostitis or ostitis or degeneration with proliferation in the joints (toxic polyarthritis or osteo-arthritis of the senile type).

But if the joint condition is purely one of the nutrition, it might be asked, Why should the joints and bones alone be involved? This question is readily answered. In the first place, the bones and joints are not the only tissues involved. In the severe forms the tissues in the neighborhood of the joints are appreciably atrophied. There is general emaciation and secondary anemia. The general musculature is markedly atrophied. That the internal organs show no changes is by no means certain; they have never been carefully examined. Finally, the fact that the bones are so strikingly involved, is not at all surprising when it is remembered that the bones are unusually sensitive to changes in the general nutrition as, for example, the marked bone changes in rachitis, the atrophy of senility, and even physiological conditions, the bone softening in puberty, juvenile osteo-arthritis, lateral curvature, etc., and the osteomalic changes in pregnant women.

From the study of metabolic osteo-arthritis here undertaken we are justified in drawing the following conclusions: (1) Metabolic osteo-arthritis is a distinct pathological condition of the joints, which can easily be recognized clinically; (2) it is not, however, a primary joint disease causing secondary general symptoms; (3) nor is a uniform specific general disease responsible for it; (4) it occurs in connection with a number of distinct clinical conditions, some of which are known to be specific diseases; (5) the joint disease is not due directly to the conditions with which it is associated, but is due to their deleterious influence upon the general nutrition.

How the metabolism is affected or what changes it undergoes has not been determined. What is certain, however, is that the changes in the joint are passive: simply an atrophy which can only be induced by inadequacy of the nutrition.

For these reasons the joint disease here discussed has been grouped with the nutritive or trophic joint diseases. In order to distinguish it from those conditions which cause local changes only it has been termed metabolic, and to distinguish it from the rather uncommon metabolic conditions which cause synovial changes only, it has been called osteo-arthritis.

Thus, metabolic osteo-arthritis is a chronic osteo-arthritis due to a vice of the metabolism caused by a number of conditions, organic or functional; insidious in onset; symmetrically involving new joints toward the trunk, it gradually leads to more or less deformation and crippling. The *x*-rays shows circumscribed bone rarefication in the early stages, and a more or less complete absorption of the epiphyses in the later stages, but never proliferation or bony ankylosis. Pathologically, beginning in the bone, there is a pure atrophic degeneration of all the joint structures.

TREATMENT. Up to the present time the prognosis in metabolic osteo-arthritis was considered hopeless as regards the recovery from the joint condition. To be sure, it was known that in certain cases the disease became quiescent; but no consistent effort to improve the condition, as far as I know, has been successful. These individuals are among those who have spent their time visiting one resort after another without deriving benefit from any. Cures have been reported, but those who recovered were evidently not suffering from metabolic osteo-arthritis.

In reporting results of treatment in these cases, the sine qua non is the diagnosis. To say one has cured a case of rheumatoid arthritis is to say nothing at all—for the case may have been one of infectious polyarthritis which could have recovered without specific treatment of any kind. So in the cases, to speak only of recent examples, reported by Hoke and Andrews, which are said to have been cured by the use of kifolac. These cases comprised all forms of joint disease, monarticular, polyarticular, trophic, and infectious, so that these statistics are practically useless. Whether or not kifolac is useful in metabolic osteo-arthritis, I have not been able to determine. In the few cases I have seen which were treated with it, I could see no improvement; but these cases were not in my own care, and apparently were not systematically treated. On the other hand, I have had uniformly good results with the use of thymus gland extract.

Some years ago I began to use it, because of the influence of the thymus upon the development of the bones, as was shown by Basch[3] in his experiments upon animals. I first used it in children in whom I found it had a very remarkable effect. In children with the metabolic osteo-arthritis with large glands and spleen, the joint disease soon became quiescent, and children who had not been upon their feet for from six months to over a year were again able to walk. That the restoration was due to the thymus and not to natural causes, was proved by the fact that the joint symptoms soon returned when the gland treatment was omitted. Good results were also obtained in children without glandular swelling, and in adults. In adults the effect upon the general nutrition is very marked. Patients who are extremely emaciated soon begin to take on flesh, and the muscular power is greatly increased. In the earlier stages of the disease the improvement is more rapid and definite. In the later stages large doses must be continued for some time before there is apparent benefit.

Of course it is quite hopeless to attempt restoration of joints which have been more or less completely absorbed. But in these cases the improvement in the general condition and increased weight is of decided benefit to the afflicted individual. In long-standing cases muscular contraction continues even after all joint symptoms have subsided. Such muscles have been permanently shortened, and the deformity so caused must be corrected by tenotomy. To attempt to stretch these tendons is dangerous, because such efforts are more likely to result in the fracture of the softened bones than in the stretching of the tendons. I have seen this accident a number of times.

My method of proceeding in these cases is as follows: The thymus is given immediately. I usually begin with two 5-grain tablets, thrice daily. In two weeks the dose is increased to three tablets, and after a few months three tablets four times a day are given. The patient is kept at rest until all symptoms of active joint disease have subsided. I then begin passive motion in all the affected joints. This is carefully done at first and gradually increased until I have an arc of free motion which is only limited by the shortened tendons. Massage, which is often painful, is unnecessary and may even be harmful. My next step is to get the patient on his feet. This is sometimes a tedious affair; for patients, particularly adults, are timid at trusting themselves at first. But by persistence the patient eventually gains confidence, and finally is able to get around as well as deformity in the lower extremity will permit. I have found it much more satisfactory, when I have the proper assistance and the patient the means, to take them into a private institution whilst they are learning to walk. Public hospitals are not suitable, because in them there are neither the trained assistants nor the time for this kind of work. A persevering intelligent mother can usually do more with a child than anyone else.

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[3] Jahrbuch f. Kinderheilkunde, Band xiv.

As soon as the patient is able to be upon his feet or use his joints without the appearance of joint irritation, all contracted tissues are divided with the tendome and the deformity is corrected. This, of course, requires immobilization for three or four weeks; but with light plaster-of-Paris bandages it does not preclude the use of the lower extremities. A few days after the operation the patient is again induced to be about, and he is usually able to hobble around quite comfortably with crutches or a cane until the bandages are removed.

With such treatment all but the most severe cases, which have existed for a long time, can be definitely improved. Often the patients recover sufficiently to be about and attend their avocations. The treatment, however, requires patience, a definite knowledge of the condition, and time; without these only in the very mild cases can one be successful.

It must not be supposed that I consider the thymus extract a specific for the cure of this condition. The nature of the disease, as it has been enunciated in this communication, precludes such an idea. Moreover, the fact that in children the enlargement of the glands, liver, and spleen is not at all affected, although the joint condition is markedly improved, shows conclusively that its action is not specific, as far as the original constitutional condition is concerned. The thymus acts simply as a stimulant to the nutritive processes, and probably in a measure counteracts the deleterious influence of the causative condition.

In conclusion, I take pleasure in thanking the following gentlemen for the use of clinical material: Dr. W. R. Townsend, Dr. V. P. Gibney, of the Hospital for Ruptured and Crippled; Dr. E. Libman and Dr. M. Manges, of the Mt. Sinai Hospital; and Dr. Albee and Dr. Cole, for *x*-ray work done for me. The majority of my cases were seen outside of hospital practice, and I am indebted to many of my medical friends for referring them to me.